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Influence of Caffeine on Serum Substrate Changes During Running  
in Trained and Untrained Individuals

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## Introduction

Previous studies have indicated that caffeine (CAF) increases the mobilization and metabolism of free fatty acids (FFA) during prolonged exercise while sparing muscle glycogen (Costill et al., 1978; Ivy et al., 1979; Essig et al., 1980). It has also been shown that differences exist between trained and untrained individuals in terms of substrate utilization and enzyme activity (Evans et al., 1979; Holloszy et al., 1975). Therefore, examining trained and untrained individuals may be a way to further elucidate the mechanism of action of CAF on lipid and carbohydrate metabolism during exercise and this was the purpose of the present study.

## Methods

Ten male subjects (5 trained runners (T) and 5 untrained individuals (UT)) volunteered to participate in this investigation after being informed of the nature and risks of the study. The T ran an average of about 32 miles a week while the UT did not exercise habitually nor had they performed any regular exercise of a long continuous nature in over three months. The average height and weight ( $\pm$  SD) of the T was  $177.3 \pm 4.5$  cm and  $70.1 \pm 7.8$  kg and that of the UT was  $175.5 \pm 4.6$  cm and  $81.5 \pm 9.8$  kg.  $\dot{V}O_2$  max of the T was  $62.4 \pm 3.0$  ml/kg/min and that of the UT was  $46.5 \pm 5.1$  ml/kg/min.

Preliminary testing consisted of a maximal oxygen uptake determination ( $\dot{V}O_{2\text{max}}$ ) and a submaximal discontinuous test to determine the onset of blood lactate accumulation (OBLA).  $\dot{V}O_2$  max was determined using an interrupted uphill running treadmill protocol. The criterion for  $\dot{V}O_{2\text{max}}$  was a change of less than 1.5 ml/kg/min in  $\dot{V}O_2$  despite a 2.5% increase in grade. One week later the OBLA was determined by having subjects run on a treadmill at 0% grade for 8-12, 4 min intervals. Near the end of each interval,  $\dot{V}O_2$  values were collected and the subject walked for two minutes while blood samples were collected and analyzed for lactates. Treadmill speeds were increased 0.8 km/hr on each successive interval and  $\dot{V}O_2$  and lactate values were

collected as above. These studies indicated that no subject began accumulating a significant amount of lactate (2 mmoles/l) until greater than 60%  $\dot{V}O_2$  max. Therefore, a speed corresponding to 60% of each subject's  $\dot{V}O_2$  max was extrapolated to within 0.4 km/hr from the  $\dot{V}O_2$  data and this speed was used in the subsequent 1 hr runs.

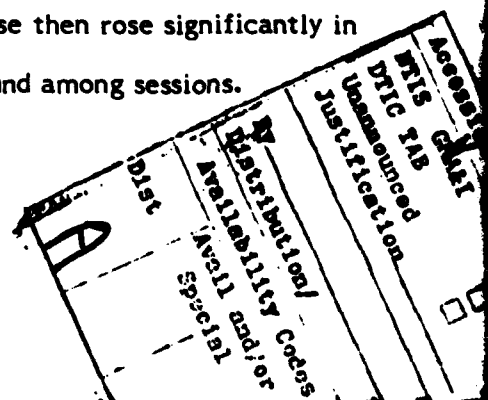
The experimental sessions consisted of three 1 hr runs separated by about two weeks each. Shortly after reporting to the laboratory subjects ingested a premixed beverage containing either 0, 5 or 9 mg/kg body weight of anhydrous caffeine dissolved in a lemon-lime flavored drink sweetened with saccharin. Administration of the beverage was conducted in a double-blind fashion. One hr after ingesting the drink, subjects began running for 1 hr at 60%  $\dot{V}O_2$  max. During the run an 11 ml blood sample was obtained from an indwelling catheter at 0 min, 5 min, and 10 min, and every subsequent 10 min. Respiratory exchange ratios (R values) were obtained at each time period just prior to blood collection.

Data were analyzed using a three way fixed model analyses of variance with repeated measures. Post hoc analysis was performed using the Tukey test. The level of statistical significance was set at  $p < 0.05$ .

### Results

Figure 1 shows the R values during the 1 hr run. The R values for the T were lower than those of the UT and they declined significantly over time; however, there were no differences among the three sessions within the two groups.

The serum and blood substrate values during the 1 hr runs are shown in figure 2. Serum glycerol values increased progressively over time. The T had higher glycerol levels than the UT except during the 9 mg/kg session. Although within each group no significant dosage effect was seen, a tendency toward higher levels was noted in the CAF sessions ( $F(2,16) = 2.86, p < .09$ ). Serum FFA declined at 5 min of exercise then rose significantly in both groups in all sessions. No significant differences were found among sessions.



Serum glucose rose significantly over time for the T but was elevated to a greater extent in the CAF sessions. In the UT a significant decline occurred over time during the placebo session. After 20 min the serum glucose of the UT during the CAF sessions was significantly elevated over that of the placebo session and this difference was maintained throughout the remainder of the exercise. Blood lactates declined significantly over time at all dosages for the T and during the placebo session for the UT. However, lactates rose in the UT during both CAF sessions.

### Discussion

Previous studies have noted that CAF stimulates mobilization and oxidation of FFA. In the present study there was a trend towards increased mobilization as suggested by the glycerol data. However, the R values did not change indicating that the effect of CAF on fat oxidation was not substantial. Previous studies have used a bicycle ergometer (Costill et al., 1978; Essig et al., 1980) or a Fitron (Ivy et al., 1979) which required a smaller muscle mass than the treadmill utilized in the present study. Any increase in circulating FFA would be distributed to this additional muscle mass and thus a significant increase in fat oxidation may not be seen. A variable that confounds this comparison of involved muscle mass is the exercise intensity used in two of the previous studies. Costill et al. (1978) had subjects exercise at 69%  $\dot{V}O_2$  max while Essig et al. (1980) used 80%  $\dot{V}O_2$  max. These were both higher than the 60%  $\dot{V}O_2$  max of our study. However, the higher exercise intensities themselves may be an alternate explanation for the differences in fat mobilization between previous studies and the present one. Higher exercise intensities are known to cause a greater epinephrine release (Terjung, 1980). While CAF stimulates epinephrine release it also potentiates the effects of existant epinephrine on FFA mobilization (Vaughan and Steinberg, 1963). Thus, the lower exercise intensity of the present study may have resulted in lower amounts of total circulating epinephrine on which CAF could exert a potentiation effect.

The dramatic increase in blood lactates seen in the UT with CAF and the higher serum glucose levels may suggest a glycogenolytic effect of CAF. CAF is known to stimulate glycogenolysis in both liver and muscle (Sutherland et al., 1968). Artificially elevated blood glucose levels induced by oral glucose ingestion increases the active muscle uptake of glucose and increases glucose oxidation during exercise (Ahlborg and Felig, 1977). Although no evidence for increased glucose oxidation was found in our study, the possibility that elevated blood glucose levels resulted in increased uptake by the muscle cannot be discounted. Regardless of whether or not increased glucose uptake occurred, the lactate accumulation seen in the UT indicates increased glycolytic flux during the CAF sessions compared to the placebo session.

The failure to show a CAF effect on lactates in the T despite elevated serum glucose levels may reflect enzymatic adaptations that occur as a result of training. Training results in less lactate accumulation at the same relative exercise intensity when rates of glycogenolysis are similar (Saltin and Karlsson, 1971). Levels of aspartate transaminase and malate dehydrogenase are higher in T (Holloszy et al., 1975). These enzymes are used in the malate-aspartate shuttle to transfer reducing compounds across the mitochondrial membrane so less need be produced in the lactate dehydrogenase (LDH) reaction. There is a reduction in total LDH in muscle with training but an increase in the heart isozyme of the enzyme (Sjodin et al., 1976). Training also results in an increase in the ability to transaminate pyruvates to alanine (Mole et al., 1973; Holloszy et al., 1975).

To summarize, there was no evidence for increased fat oxidation in the present study. However, there was some suggestion of increased glycogenolysis. The elevated serum glucose levels during the CAF sessions indicated increased liver glycogenolysis. The higher blood lactate and serum glucose levels in the UT during the CAF sessions suggested an increased glycolytic flux in the active muscles. While the elevated serum glucose levels may also indicate increased glycolytic flux in the T, the failure to find lactate accumulation in this group may reflect enzymatic adaptations induced by training.

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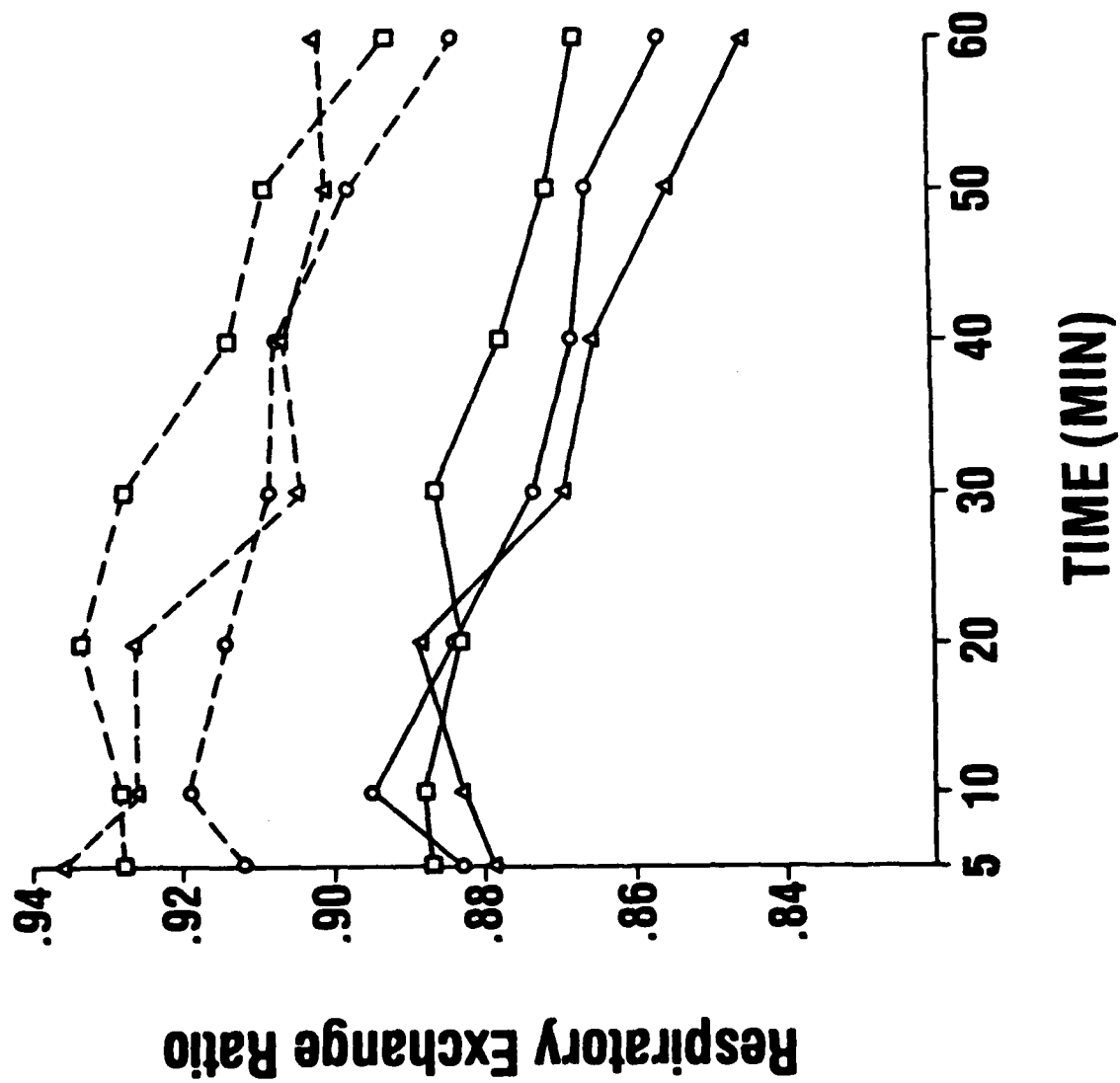
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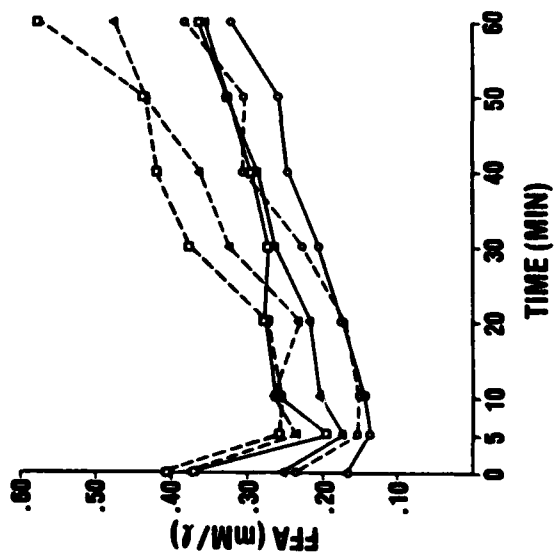
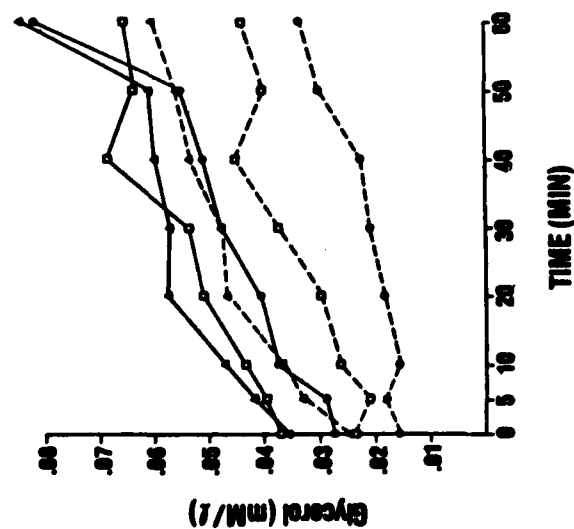
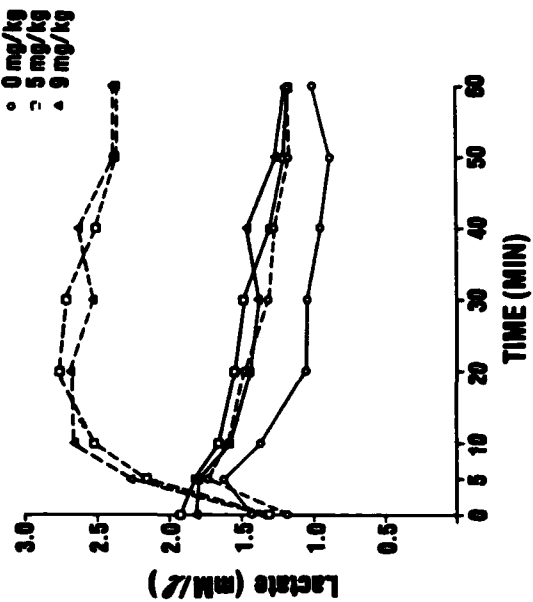
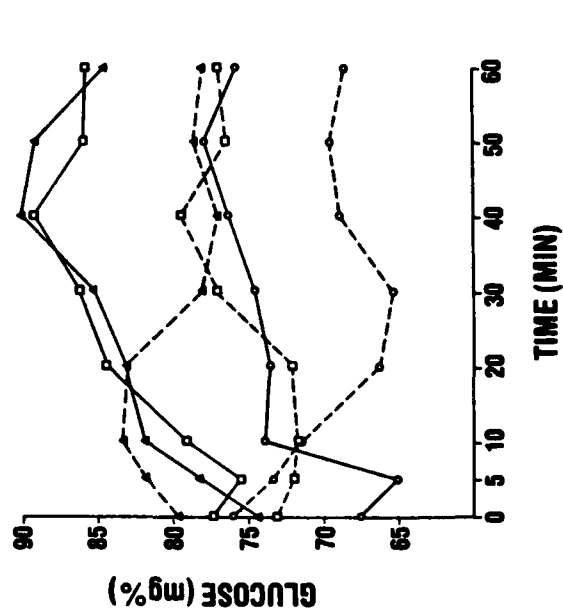
## Figure Legends

Figure 1. Respiratory Exchange Ratios During the 1 hr Run.

Figure 2. Serum and Blood Substrate Parameters During the 1 hr Run.

— T  
 - - UT  
 ○ 0 mg/kg  
 □ 5 mg/kg  
 △ 9 mg/kg





The views, opinions, and/or findings contained in this report are those of the author(s) and should not be construed as an official department of the Army position, policy, or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Previous research has indicated that caffeine (CAF) increases the mobilization and metabolism of free fatty acids (FFA) during prolonged exercise while sparing muscle glycogen. The purpose of this study was to examine the effect of two dosages of CAF on serum substrates in trained (T) and untrained (UT) subjects. In a double blinded, cross-over design, 5 T subjects ( $VO_2 \text{ max} = 62.4 \pm 3.0 \text{ ml/kg/min}$ ) and 5 UT subjects ( $VO_2 \text{ max} = 46.5 \pm 5.1 \text{ ml/kg/min}$ ) ran for 1 hr in 3 separate sessions, 1 h after ingestion of a beverage containing either 0, 5 or 9 mg/kg body weight of anhydrous caffeine. Initial exercise intensities were 59%		

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20. Abstract (continued)

VO<sub>2</sub> max (T) or 61% VO<sub>2</sub> max (UT). Blood samples were collected from an indwelling catheter just prior to the run, and at min 5, 10 and every 10 min thereafter. Serum glycerol levels did not differ following CAF ingestion in T or UT as compared to the placebo, though a trend toward higher levels was observed with CAF. Serum FFA increased progressively during the exercise period; however there were no differences ( $p > 0.05$ ) associated with CAF in either T or UT. Serum glucose decreased in the UT during the placebo session and increased in the T during the CAF sessions. Blood lactates were significantly elevated ( $p < 0.05$ ) in the UT in both the 5 mg/kg (2.36 - 2.77 mmol/l) and 9 mg/kg (2.38 - 2.68 mmol/l) dosages as compared to the placebo (1.17 - 1.60 mmol/l); however this CAF effect on lactate values was not seen in the T. These results suggest that the effects of CAF on fat metabolism during exercise in both T and UT are not substantial though the effects on glycogenolysis may be more pronounced. This is especially evident in the UT whose capacity for handling lactate is limited.

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